DETAILED ACTION

Election/Restrictions

1. Applicant's election of the species "skin aging" and "crèmes" in the reply filed on 3/5/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The restriction requirement is therefore deemed proper and is made FINAL.

2. Claims 1-18 are currently pending and are the subject of this office action.

Information Disclosure Statement

The information disclosure received on 11/18/2005 has been fully considered.

Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of reducing UV-induced DNA damage, does not reasonably provide enablement for methods of preventing or treating any disorder associated with damage induced by UV radiation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered when determining if the disclosure satisfies the enablement requirement have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the

breath of claims. Ex Parte Forman, (230 USPQ 546 (Bd. Pat. App. & Int. 1986); In re Wands, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The claims of the instant invention are drawn to methods of preventing or treating disorders of the skin associated with damage induced by UV radiation by administering to a patient in need an effective amount of IL-18. The claims are further drawn to treating or preventing disorders such as sunburn, inflammation, skin aging, and skin cancer, or skin disorders associated with apoptosis, and to disorders associated with exposure to various wavelengths of UV radiation. As written, the claims read broadly on treatment of any condition associated with UV radiation, or of preventing all possible conditions associated with UV radiation. Given the broadest reasonable interpretation, all subjects could be considered to be in need of prevention of skin disorders associated with UV radiation, and prevention can be interpreted as prophylaxis. Although the specification provides details of an experiment showing administration of IL-18 30 minutes prior to UV radiation exposure decreased DNA damage, there is no guidance or examples showing how to prevent, in all possible patient populations, all types of disorders of the skin associated with UV radiation. Given that many skin disorders can be considered to be "associated" with UV radiation because virtually all individuals are exposed to UV radiation on a daily basis, one of ordinary skill in the art would not be able to predict which disorders could be prevented by the claimed methods. For example, psoriasis or acne could be considered to be "associated with" UV radiation because patients suffering from these conditions would be expected to be exposed to some degree of UV radiation. However, there is no guidance or examples in the specification or the art showing that these disorders, or any other specific disorder, can be actually prevented by administration of IL-18.

Furthermore, there is no guidance or examples of any actual treatment of any disorder. The claims read broadly on treatment of disorders such as any type of inflammation caused by UV-induced DNA damage, and also recite treatment of skin cancer. One of ordinary skill in the art would expect, however, that established cases of skin cancer, for example, would have already suffered UV-induced DNA damage, and would not predict that the claimed methods would be effective in treating skin cancer, or any type of inflammation, in which the DNA damage had already occurred.

Therefore, due to the excessive breadth of the claims, which read on prophylaxis or complete prevention of all possible disorders associated with UV radiation, in all possible patient populations, and the lack of guidance in the specification showing how to completely prevent or treat these disorders, one of ordinary skill in the art would require further, undue experimentation in order to practice the instant invention in manner commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 1-11, 13, and 15-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Osaki *et al* ("Osaki" - *J. Immunol.*, 1998, Vol. 160, p. 1742-1749). The claims of the instant invention are drawn to methods of preventing or treating a disorder of the skin associated with damage induced by UV radiation, wherein said method comprises administration of an effective amount of IL-18. The claims are further drawn to administration of various doses of IL-18 and via various routes of administration, for prevention or treatment of disorders such as sunburn, inflammation, skin cancer, skin aging, and disorders associated with apoptosis.

Osaki teaches administration of IL-18 to mice for treatment of melanoma (p. 1743, 1st column, 2nd paragraph). Osaki specifically teaches intraperitoneal administration of IL-18 at various doses, including 1 μg once a day (see p. 1743, 2nd column, 1st paragraph). Although Osaki does not explicitly teach treatment of a disorder of the skin associated with damage induced by UV radiation, the claims of the instant invention read on method of *preventing* such disorders. Because the claims recite prevention in a patient in need of such treatment and all subjects can be considered as being in need of preventing skin damage induced by UV radiation, and prevention can be interpreted as prophylaxis, the method of Osaki can be considered as a method of preventing disorders of the skin associated with damage induced by UV radiation, including disorders such as sunburn, inflammation, skin aging, skin cancer, and disorders associated with apoptosis or alleviated and/or prevented by induction of the NER pathway. Thus, Osaki meets the limitations of claims 1-4, 10-11, and 15-16 of the instant application because the method would inherently prevent the claimed disorders, and the IL-18 is systemically administered, via intraperitoneal injection, once a day at a dosage of 1 μg. Furthermore, the method of Osaki can be considered a method of preventing disorders arising from exposure to any wavelength of UV radiation, including those recited in claims 5-8, and UV radiation originating from natural and/or artificial sunlight. In the absence of a

preferred definition of "artificial sunlight", the lights in the laboratory in which the studies were conducted could be considered as artificial light sources, and therefore the mice would be expected to have been exposed to artificial sunlight, thus meeting the limitations of claims 5-8

2. Claims 1-13 and 15-18 are rejected under 35 U.S.C. 102(e) as being anticipated by Gillispie *et al* ("Gillispie" – US 6,896,880).

The subject matter of the instant invention is discussed *supra*. Gillispie teaches administration of IL-18 for treatment of diseases associated with excessive osteoclast formation or activity (see claims 1-5). Gillispie teaches that the IL-18 can be administered by several routes, including intradermally, subcutaneously, muscularly, or intravenously, once a day, and at doses of 0.5 μg to 100 mg (column 5, lines 36-44). Although Gillispie does not explicitly teach treatment of a disorder of the skin associated with damage induced by UV radiation, the claims of the instant invention read on method of *preventing* such disorders. Because the claims recite prevention in a patient in need of such treatment and all subjects can be considered as being in need of preventing skin damage induced by UV radiation, and prevention can be interpreted as prophylaxis, the method of Gillispie can be considered as a method of preventing disorders of the skin associated with damage induced by UV radiation, including disorders such as sunburn, inflammation, skin aging, skin cancer, and disorders associated with apoptosis or alleviated and/or prevented by induction of the NER pathway. Thus, Gillispie meets the limitations of claims 1-4, 9-13, and 15-18 of the instant application because the method would inherently prevent the claimed disorders, and the IL-18 is systemically administered to humans, via intradermal or subcutaneous injection, once a day at dosages encompassing the claimed range. Furthermore, because the method of Gillispie can be considered a method of preventing disorders arising from exposure to any wavelength of UV radiation, including those recited in claims 5-8 and UV radiation originating from natural and/or artificial sunlight, and a human subject would be expected to be exposed to natural or artificial sunlight, Gillispie meets the limitations of claims 5-8.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill

in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Osaki *et al.* The subject matter of the instant application and the teachings of Osaki are discussed *supra*. Claim 14 is further drawn to administration of IL-18 at a dose range of from 0.1 μg/kg bodyweight to 100 μg/kg bodyweight. Although Osaki does not explicitly teach administration of IL-18 at this dosage, it would have been obvious to one of ordinary skill in the art to optimize the dosage of IL-18 in order to practice the most effective method of treating melanoma. MPEP 2144.05 states:

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 454, 105 USPQ 223, 235, (CCPA 1955).

In the instant case, Osaki discloses the general conditions of a method that can be considered as *preventing* disorders of the skin associated with damage induced by UV radiation, as discussed in the rejection under 35 USC 102(b). Therefore, one of ordinary skill in the art would have the motivation to optimize the dosage of IL-18 for administration in a method that would inherently prevent the recited disorders.

2. Claim 14 rejected under 35 U.S.C. 103(a) as being unpatentable over Gillispie *et al.* The subject matter of the instant application and the teachings of Gillispie are discussed *supra*. Claim 14 is further drawn to administration of IL-18 at a dose range of from 0.1 μg/kg bodyweight to 100 μg/kg bodyweight. Although Gillispie does not explicitly teach administration of IL-18 at this dosage, it would have been obvious to one of ordinary skill in the art to optimize the dosage of IL-18 in order to practice the most effective method of treating melanoma. MPEP 2144.05 states:

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 454, 105 USPQ 223, 235, (CCPA 1955).

In the instant case, Gillispie discloses the general conditions of a method that can be considered as *preventing* disorders of the skin associated with damage induced by UV radiation, as discussed in the rejection under 35 USC 102(e). Therefore, one of ordinary skill in the art would have the motivation to optimize the dosage of IL-18 for administration in a method that would inherently prevent the recited disorders.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571)272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bruce D. Hissong
Art Unit 1646

/Robert Landsman/
Primary Examiner, Art Unit 1647